

M-I (2) Non-technical abstract. Cardiovascular disease is the single leading cause of mortality in the United States, responsible for the deaths of two out of every five Americans, with a total of nearly one million deaths annually. Coronary artery disease describes a broad spectrum of ischemic syndromes that may evolve from atherosclerosis, thrombosis, and/or vasospasm. Current therapies include pharmacologic interventions and surgical therapy by mechanical revascularization using percutaneous transluminal coronary angioplasty (PTCA), coronary artery bypass grafting (CABG), off-pump coronary artery bypass surgery (OPCAB) or transmyocardial laser revascularization (TMR). The identification of specific biologic mediators of angiogenesis make it possible to consider "therapeutic angiogenesis," where angiogenic molecules can be employed to develop new vascular networks to circumvent the ischemic consequences of atherosclerosis occluding the arterial system. The most specific of the known angiogenic indicators is vascular endothelial growth factor (VEGF). The focus of this protocol is the delivery of VEGF cDNA directly into the myocardium of individuals with life threatening coronary artery disease in conjunction with coronary artery bypass surgery. The rationale behind this study is that by injecting the VEGF expression cassette directly into the heart we can improve myocardial blood flow/function as assessed by using exercise tolerance testing, ^{99m}Tc-sestamibi single photon emission computerized tomography (SPECT) scan and a magnetic resonance imaging (MRI) scan. The protocol will include 50 individuals, each with clinically significant coronary artery disease, and will be divided into two groups by chance (by 'flip of the coin'). One group will receive the Ad_{CU} VEGF121.1 vector and the other will receive the placebo (a salt-carbohydrate solution in which the vector will be diluted). At the conclusion of the study, the following objectives will be met: (1) to determine the safety/toxicity of direct administration of the vector Ad_{CU} VEGF121.1 to the ischemic myocardium; (2) to assess whether direct administration of Ad_{CU} VEGF121.1 to the myocardium will induce growth of collateral blood vessels, improve coronary blood flow and improve cardiac function in the region of ischemia in individuals with coronary artery disease undergoing OPCAB.